4		Search Text	DB	Time stamp
	10	(method or administer?) with VEGF with (variant or mutant or	USPAT;	2004/06/14 12:11
		mutation or agonist) with KDR	US-PGPUB;	
		, ,	EPO; JPO;	
			DERWENT	
5	270	kdr adj receptor\$	USPAT;	2004/06/14 12:12
			US-PGPUB;	
			EPO; JPO;	
			DERWENT	
6	80	vegf adj variant	USPAT;	2004/06/14 12:12
			US-PGPUB;	
			EPO; JPO;	
			DERWENT	
7	7	vegf adj receptor adj agonist	USPAT;	2004/06/14 12:12
			US-PGPUB;	
			EPO; JPO;	
}			DERWENT	
8	7	vegf adj receptor\$ adj agonist\$	USPAT;	2004/06/14 12:13
		, , , , , , , , , , , , , , , , , , , ,	US-PGPUB;	200 17007 17 12:10
			EPO; JPO;	
			DERWENT	
9	554	(kdr adj receptor\$) smae (vegf adj variant) same (vegf adj	USPAT;	2004/06/14 12:13
		receptor\$ adj agonist\$)	US-PGPUB;	
			EPO; JPO;	
			DERWENT	
10	0	(kdr adj receptor\$) same (vegf adj variant) same (vegf adj	USPAT;	2004/06/14 12:13
		receptor\$ adj agonist\$)	US-PGPUB;	200 ,,00,11 12:10
			EPO; JPO;	
			DERWENT	
11 .	7	(kdr adj receptor\$) same ((vegf adj variant) or (vegf adj	USPAT;	2004/06/14 12:13
		receptor adj agonist))	US-PGPUB;	
		, , , , , , , , , , , , , , , , , , , ,	EPO; JPO;	
			DERWENT	
15	87	vegf with (amino adj acid) with (substitution\$ or modification\$	USPAT;	2004/06/14 12:52
		or change\$ or conversion\$)	US-PGPUB	
16	8	(d63s or d63 or asp63 or g65m or gly65 or g65 or l66r or	USPAT;	2004/06/14 12:55
		leu66 or "l66") with vegf	US-PGPUB	
17	6	(vegf adj variant) same (kdr adj receptor\$)	USPAT;	2004/06/14 12:55
			US-PGPUB	
-	10	shen-ben\$.IN.	USPAT;	2003/12/10 14:28
			US-PGPUB;	
			EPO;	
		·	DERWENT	
-	11	zioncheck-t\$.IN.	USPAT;	2003/12/10 11:35
]			US-PGPUB	
			EPO;	
			DERWENT	
-	7452	vascular adj endothelial adj growth adj factor or vegf	USPAT;	2003/12/10 11:36
			US-PGPUB;	
			EPO;	
			DERWENT	
-	215360	variant or agonist	USPAT;	2003/12/10 11:37
			US-PGPUB;	
			EPO;	
			DERWENT	
-	579	(vascular adj endothelial adj growth adj factor or vegf) with	USPAT;	2003/12/10 11:37
1		(variant or agonist)	US-PGPUB;	
			EPO;	
			DERWENT	
-	857	(vascular adj endothelial adj growth adj factor or vegf) same	USPAT;	2003/12/10 11:37
		(variant or agonist)	US-PGPUB;	
			EPO;	
			DERWENT	

-	220353	(treating or treatment or prevention or preventing) with	USPAT;	2003/12/10 11:38
		(disease or disorder)	US-PGPUB;	
			EPO;	
			DERWENT	
-	3	(((treating or treatment or prevention or preventing) with	USPAT;	2003/12/10 11:38
	}	(disease or disorder)) same ((vascular adj endothelial adj	US-PGPUB;	
		growth adj factor or vegf) same (variant or agonist))) and	EPO;	
		administer?	DERWENT	
_	148	((treating or treatment or prevention or preventing) with	USPAT:	2003/12/10 12:12
		(disease or disorder)) same ((vascular adj endothelial adj	US-PGPUB;	
		growth adj factor or vegf) same (variant or agonist))	EPO;	
		3, (	DERWENT	
-	1	"9820027"	USPAT;	2003/12/10 11:49
			US-PGPUB	2000/12/10 11:10
_	2	barker-s\$.IN. and martin-j\$.IN.	USPAT;	2003/12/10 11:50
	_	January Januar	US-PGPUB	2000/12/10 11.00
_	6	barker-s\$.IN. and martin-j\$.IN.	USPAT;	2003/12/10 11:52
		barror op.n.t. and martin jo.n.t.	US-PGPUB;	2003/12/10 11.32
			EPO;	
			DERWENT	
_	2	5955311.PN.	USPAT;	2003/12/10 11:52
	-		US-PGPUB;	2003/12/10 11.32
			EPO;	
			DERWENT	
_	34	((treating or treatment or prevention or preventing) with	USPAT;	2002/12/10 12:12
		(disease or disorder)) same ((vascular adj endothelial adj	US-PGPUB;	2003/12/10 12:13
		growth adj factor or vegf) same (variant or agonist)) and		
		(kinase adj domain adj region or kdr)	EPO;   DERWENT	
_	2		USPAT;	2002/12/10 14:22
		0020470.114.	US-PGPUB;	2003/12/10 14:32
			EPO;	
			DERWENT	
_	2	6057428.PN.	USPAT;	2002/42/40 44:22
_		0037420.114.		2003/12/10 14:33
			US-PGPUB;	
			EPO;	
_	2	6592788.PN.	DERWENT	2002/40/40 44:25
_		0092700.114.	USPAT;	2003/12/10 14:35
			US-PGPUB;	
			EPO;	
	0	vegf adj mutagenesis	DERWENT	0000/40/40 44:05
		vegi auj mutagenesis	USPAT; US-PGPUB:	2003/12/10 14:35
			EPO;	
_	118	vegf same mutagenesis	DERWENT	2002/40/40 44:05
=	110	Vegi same mulagenesis	USPAT;	2003/12/10 14:35
			US-PGPUB;	
			EPO;   DERWENT	
_	5	"9708313"		2002/42/40 44:05
_		9700010	USPAT;	2003/12/10 14:35
			US-PGPUB;	
			EPO;	
		1		1

Connecting via Winsock to STN

```
Welcome to STN International! Enter x:x
```

LOGINID: SSSPTA1647RBK

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

```
* * * * * * * * *
                    Welcome to STN International
NEWS 1
                Web Page URLs for STN Seminar Schedule - N. America
                "Ask CAS" for self-help around the clock
NEWS 2
                Source of Registration (SR) information in REGISTRY updated
NEWS 3 JAN 27
                and searchable
NEWS 4 JAN 27 A new search aid, the Company Name Thesaurus, available in
                CA/CAplus
NEWS 5 FEB 05 German (DE) application and patent publication number format
                changes
NEWS 6 MAR 03 MEDLINE and LMEDLINE reloaded
NEWS 7 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 8 MAR 03 FRANCEPAT now available on STN
NEWS 9 MAR 29 Pharmaceutical Substances (PS) now available on STN
NEWS 10 MAR 29 WPIFV now available on STN
NEWS 11 MAR 29 New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12 APR 26 PROMT: New display field available
NEWS 13 APR 26 IFIPAT/IFIUDB/IFICDB: New super search and display field
                available
NEWS 14 APR 26 LITALERT now available on STN
NEWS 15 APR 27
                NLDB: New search and display fields available
NEWS 16 May 10 PROUSDDR now available on STN
NEWS 17 May 19 PROUSDDR: One FREE connect hour, per account, in both May
                and June 2004
NEWS 18 May 12 EXTEND option available in structure searching
                Polymer links for the POLYLINK command completed in REGISTRY
NEWS 19 May 12
NEWS 20 May 17
                FRFULL now available on STN
                STN User Update to be held June 7 and June 8 at the SLA 2004
NEWS 21 May 27
                Conference
NEWS 22 May 27
                New UPM (Update Code Maximum) field for more efficient patent
                SDIs in CAplus
                CAplus super roles and document types searchable in REGISTRY
NEWS 23 May 27
NEWS 24 May 27 Explore APOLLIT with free connect time in June 2004
NEWS EXPRESS MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
             MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
             AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS
             STN Operating Hours Plus Help Desk Availability
             General Internet Information
NEWS INTER
             Welcome Banner and News Items
NEWS LOGIN
NEWS PHONE
             Direct Dial and Telecommunication Network Access to STN
NEWS WWW
             CAS World Wide Web Site (general information)
```

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer

agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

FILE 'HOME' ENTERED AT 13:38:21 ON 14 JUN 2004

=> file medline caplus scisearch biosis uspatfull pctfull COST IN U.S. DOLLARS SINCE FILE

ENTRY SESSION

TOTAI.

FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 13:38:43 ON 14 JUN 2004

FILE 'CAPLUS' ENTERED AT 13:38:43 ON 14 JUN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'SCISEARCH' ENTERED AT 13:38:43 ON 14 JUN 2004 COPYRIGHT 2004 THOMSON ISI

FILE 'BIOSIS' ENTERED AT 13:38:43 ON 14 JUN 2004 COPYRIGHT (C) 2004 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'USPATFULL' ENTERED AT 13:38:43 ON 14 JUN 2004 CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'PCTFULL' ENTERED AT 13:38:43 ON 14 JUN 2004 COPYRIGHT (C) 2004 Univentio

=> s kdr(w)receptor? L1 880 KDR(W) RECEPTOR?

=> s vegf(3a)variant?

L3 777 VEGF(3A) VARIANT?

=> s 11(s)(12 or 13)

L4 21 L1(S)(L2 OR L3)

=> dup rem 14

PROCESSING COMPLETED FOR L4

L5 17 DUP REM L4 (4 DUPLICATES REMOVED)

=> d ibib abs 1-17

L5 ANSWER 1 OF 17 USPATFULL on STN

ACCESSION NUMBER:

2004:44956 USPATFULL

TITLE: INVENTOR(S):

Use of VEGF for treating bone defects

Bunting, Stuart, Half Moon Bay, CA, UNITED STATES Carano, Richard, San Ramon, CA, UNITED STATES

Filvaroff, Ellen Hope, San Francisco, CA, UNITED STATES Gosselin, Richard Andre, El Granada, CA, UNITED STATES Peale, Franklin V., JR., San Carlos, CA, UNITED STATES

PATENT ASSIGNEE(S): GENENTECH, INC. (U.S. corporation)

NUMBER KIND DATE PATENT INFORMATION: US 2004033949 A1 20040219 APPLICATION INFO.: US 2003-431105 A1 20030506 (10)

NUMBER DATE -----

PRIORITY INFORMATION: US 2002-378275P 20020506 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: GENENTECH, INC., 1 DNA WAY, SOUTH SAN FRANCISCO, CA,

94080

NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 1650 NUMBER OF CLAIMS:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides pharmaceutical compositions comprising VEGF or variants thereof for promoting bone formation, in vitro and in vivo. Methods of using those compositions are also provided. Compositions and methods of the present invention can be used for promoting and improving the repair process in subjects with bone

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 2 OF 17 USPATFULL on STN

ACCESSION NUMBER: 2004:103582 USPATFULL

Medical articles prepared for cell adhesion TITLE: Carlyle, Wenda C., Petaluma, CA, United States Brendzel, Avrom M., Roseville, MN, United States INVENTOR(S):

St. Jude Medical, Inc., United States (U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER KIND DATE -----

PATENT INFORMATION: US 6726718 B1 20040427
APPLICATION INFO.: US 1999-459451 19991213 (9)
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Willse, David H.
ASSISTANT EXAMINER: Blanco, Javier G.
LEGAL REPRESENTATIVE: Altera Law Group, LLC, Finucane, Hallie A.
NUMBER OF CLAIMS: 35

NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Figure(s); 16 Drawing Page(s)
1.TNE COUNT: 1256

LINE COUNT: 1256

A prosthesis is formed from a biocompatible material having one or more associated cell adhesion stimulating proteins. The biocompatible material can be a ceramic material or a carbon coated material. The cell adhesion stimulating protein can be a structural protein or a polypeptide growth factor, such as vascular endothelial growth factor. Viable cells can be adhered in vivo or in vitro to the biocompatible material with the cell adhesion stimulating protein.

ANSWER 3 OF 17 USPATFULL on STN

ACCESSION NUMBER: 2003:135058 USPATFULL

Medical devices that stimulate growth factor production TITLE:

Ogle, Matthew F., Oronoco, MN, UNITED STATES INVENTOR(S): McConico, Andrea L., Fridley, MN, UNITED STATES

NUMBER KIND DATE -----PATENT INFORMATION: APPLICATION INFO.: US 2003093147 A1 20030515 US 2001-8430 A1 20011113 (10)

DOCUMENT TYPE: FILE SEGMENT: Utility APPLICATION FILE SEGMENT:

LEGAL REPRESENTATIVE: PATTERSON, THUENTE, SKAAR & CHRISTENSEN, P.A., 4800 IDS

CENTER, 80 SOUTH 8TH STREET, MINNEAPOLIS, MN,

55402-2100

35 NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 1356 NUMBER OF CLAIMS:

LINE COUNT: 1356

Medical devices are described that have a releasable quantity of a stimulation compound that stimulates production of VEGF. The stimulation compound can be a polypeptide, such as hypoxia-inducible factor 1. Suitable stimulation compounds stimulate transcription of VEGF. Medical devices of particular interest include, for example, heart valve prostheses, vascular prostheses and vascular stents.

ANSWER 4 OF 17 USPATFULL on STN

ACCESSION NUMBER: 2003:128022 USPATFULL

TITLE: Treatment protocol generation for diseases related to

angiogenesis

Agur, Zvia, Tel Aviv, ISRAEL INVENTOR (S):

Arakelyan, Levon, Ashdod, ISRAEL

Vainstein, Vladimir, Jerusalem, ISRAEL

NUMBER KIND DATE \_\_\_\_\_\_ PATENT INFORMATION: US 2003088237 A1 20030508 APPLICATION INFO.: US 2002-207772 A1 20020731 (10)

NUMBER DATE -----

PRIORITY INFORMATION: US 2001-330929P 20011102 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: SUGHRUE MION, PLLC, 2100 Pennsylvania Avenue, N.W.,

Washington, DC, 20037-3213

Washington, DC, 20
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Page(s)
LINE COUNT: 1023

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A computer-implemented method for determining an optimal treatment protocol for a disease related to angiogenesis, comprising creating an angiogenesis model including pro-angiogenesis and anti-angiogenesis factors. Effective vessel density (EVD) is incorporated as a factor regulating switching on and switching off of at least one component in the angiogenesis model. Effects of vasculature maturation and mature vessels destabilization are incorporated. Pro-angiogenesis and anti-angiogenesis factors, which can influence changes in state of a tissue are selected. Effects of drugs in the pro-angiogenesis and anti-angiogenesis factors are incorporated. A plurality of treatment protocols in a protocol space is generated. A best treatment protocol based on a pre-determined criteria.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 5 OF 17 USPATFULL on STN

ACCESSION NUMBER: 2003:38104 USPATFULL TITLE: VEGF fusion proteins

INVENTOR(S): Kovesdi, Imre, Rockville, MD, UNITED STATES

Kessler, Paul D., Frederick, MD, UNITED STATES

GenVec, Inc., Gaithersburg, MD, UNITED STATES, 20878 PATENT ASSIGNEE(S):

(U.S. corporation)

NUMBER KIND DATE

US 2003027751 A1 20030206 PATENT INFORMATION: US 2001-832355 Al 20010410 (9) APPLICATION INFO .:

Utility DOCUMENT TYPE: FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: LEYDIG VOIT & MAYER, LTD, TWO PRUDENTIAL PLAZA, SUITE

4900, 180 NORTH STETSON AVENUE, CHICAGO, IL, 60601-6780

NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1 7034 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention provides therapeutic fusion proteins which include a first AΒ peptide portion comprising a first non-heparin binding VEGF peptide portion and a second non-VEGF peptide portion covalently associated with the first peptide portion, which first and second peptide portions separately promote angiogenesis, bone growth, wound healing, or any combination thereof. Further provided are polynucleotides encoding such fusion proteins, vectors including such polynucleotides, methods of making such proteins, and methods of promoting angiogenesis, bone growth, and/or wound healing using such proteins, polynucleotides, and vectors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PCTFULL COPYRIGHT 2004 Univentio on STN ANSWER 6 OF 17 ACCESSION NUMBER: 2003103581 PCTFULL ED 20040102 EW 200351

COMPOSITIONS AND METHODS FOR LIVER GROWTH AND LIVER TITLE (ENGLISH):

PROTECTION

COMPOSITIONS ET METHODES DE CROISSANCE ET DE PROTECTION TITLE (FRENCH):

DU FOIE

FERRARA, Napoleone, 2090 Pacific Avenue, #704, San INVENTOR(S):

Franicsco, CA 94109, US [US, US];

HILLAN, Kenneth, J., 64 Seward Street, San Francisco,

CA 94114, US [GB, US];

LE COUTER, Jennifer, 585 Page Street, Apt. #1, San

Francisco, CA 94117, US [CA, US]

GENENTECH, INC., 1 DNA Way, South San Francisco, CA PATENT ASSIGNEE(S): 94080-4990, US [US, US], for all designates States

except US;

FERRARA, Napoleone, 2090 Pacific Avenue, #704, San

Franicsco, CA 94109, US [US, US], for US only;

HILLAN, Kenneth, J., 64 Seward Street, San Francisco,

CA 94114, US [GB, US], for US only;

LE COUTER, Jennifer, 585 Page Street, Apt. #1, San

Francisco, CA 94117, US [CA, US], for US only

CUI, Steven X.\$, Genentech, Inc., 1 DNA Way, South San

Francisco, CA 94080-4990\$, US

LANGUAGE OF FILING: LANGUAGE OF PUBL.:

English English Patent

DOCUMENT TYPE: PATENT INFORMATION:

AGENT:

	NUMBER	KIND	DATE				
DESIGNATED STATES	WO 2003103581	A2 200	031218				
W:	AE AG AL AM AT	AU AZ BA BB	BG BR BY BZ CA CH CN CO CR				
			FI GB GD GE GH GM HR HU ID				
			LC LK LR LS LT LU LV MA MD				
			OM PH PL PT RO RU SC SD SE				
RW (ARIPO):	ZW  GH GM KE LS MW		UA UG US UZ VC VN YU ZA ZM				
RW (EAPO):	AM AZ BY KG KZ						
RW (EPO):			ES FI FR GB GR HU IE IT LU				
	MC NL PT RO SE						
RW (OAPI):			GW ML MR NE SN TD TG				
APPLICATION INFO.:	WO 2003-US17591						
PRIORITY INFO.:	US 2002-60/386		020605				
			al compositions and methods cifically useful are VEGFR				
			r growth. Disclosed				
			promoting proliferation or				
treating patholo	gical conditions	s in other or	rgans of significant				
biological funct			<i>5</i>				
		itions pharma	aceutiques ainsi que des				
methodes de rege							
	particulierement, l'invention fait intervenir des agents de modulation						
			liales (VEGFR) qui sont				
			es compositions et les				
			tiver la regeneration ou a es organes qui remplissent				
d'importantes fo			cs organics dar remprisserie				
G 1po10d11005 1.		1					
L5 ANSWER 7 OF 17	PCTFULL COP	YRIGHT 2004 U	Univentio on STN				
ACCESSION NUMBER:	2003094617 PCTI						
TITLE (ENGLISH):	USE OF VEGF FOR TREATING BONE DEFECTS						
TITLE (FRENCH):	UTILISATION DE VEGF POUR TRAITER DES DEFAUTS OSSEUX						
INVENTOR(S):		BUNTING, Stuart, 220 Miramontes Avenue, Half Moon Bay,					
	CA 94019, US; FILVAROFF, Ellen Hope, 538 18th Avenue, San Francisco,						
	CA 94121, US;	on nope, 550	Total Avenue, buil Translibed,				
		anklin V., 41	16 Pearl Avenue, San Carlos,				
	CA 94070, US;	,	· ·				
	CARANO, Richard, 2470 Paddock Drive, San Ramon, CA						
	94583, US;						
	•	-	43 Ferdinand Avenue, El	•			
DAMENT AGGIGNER (G)	Granada, CA 94		Couth Can Emandiago CA				
PATENT ASSIGNEE(S):	GENENTECH, INC., 1 DNA Way, South San Francisco, CA 94080-4990, US [US, US] CUI, Steven X.\$, GENENTECH, INC., 1 DNA Way, South San						
AGENT:	Francisco, CA						
LANGUAGE OF FILING:	English	22000 233047	<u></u>				
LANGUAGE OF PUBL.:	English						
DOCUMENT TYPE:	Patent						
PATENT INFORMATION:							
	NUMBER	KIND	DATE				
	110 0003004617		021120				
	WO 2003094617	A2 200	031120				
DESIGNATED STATES W:	ልድ ልር አ፣ አM አሞ	Δ11 Δ7 B2 BB	BG BR BY BZ CA CH CN CO CR				
vv .			FI GB GD GE GH GM HR HU ID				
			LC LK LR LS LT LU LV MA MD				

```
RW (ARIPO):
                       GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
      RW (EAPO):
                       AM AZ BY KG KZ MD RU TJ TM
      RW (EPO):
                       AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU
                       MC NL PT RO SE SI SK TR
                       BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
      RW (OAPI):
APPLICATION INFO.:
                       WO 2003-US14090 A 20030506
PRIORITY INFO.:
                       US 2002-60/378,275
                                               20020506
ABEN
      The present invention provides pharmaceutical compositions comprising
      VEGF or variants thereof for promoting bone formation, <i>in vitro</i>
      and <i>in vivo</i>. Methods of using those compositions are also
      provided. Compositions and methods of the present invention can be used
      for promoting and improving the repair process in subjects with bone
      defects.
      L'invention concerne des compositions pharmaceutiques comprenant VEGF ou
ABFR
      ses variants, lesquelles compositions permettant de favoriser la
      formation osseuse, <i>in vitro</i> et <i>in vivo</i>. L'invention
      concerne des methodes d'utilisation de ces compositions. Les
      compositions et les methodes de l'invention peuvent etre utilisees pour
       favoriser et pour ameliorer le processus de reparation chez des sujets
      presentant des defauts osseux.
                                  COPYRIGHT 2004 Univentio on STN
      ANSWER 8 OF 17
                        PCTFULL
ACCESSION NUMBER:
                       2003036410 PCTFULL ED 20030512 EW 200318
TITLE (ENGLISH):
                       TREATMENT PROTOCOL GENERATION FOR DISEASES RELATED TO
                       ANGIOGENESIS
                       CREATION D'UN PROTOCOLE DE TRAITEMENT DE MALADIES
TITLE (FRENCH):
                       ASSOCIEES A L'ANGIOGENESE
                       AGUR, Zvia, Tuval St, 11, 52522 Ramat-Gan, IL [IL, IL];
INVENTOR(S):
                       ARAKELYAN, Levon, Tuval St, 11, 52522 Ramat-Gan, IL
                        [IL, IL];
                       VAINSTEIN, Vladimir, Tuval St, 11, 52522 Ramat-Gan, IL
                        [IL, IL]
                       OPTIMATA LTD., Tuval St, 11, 52522 Ramat-Gan, IL [IL,
PATENT ASSIGNEE(S):
                       IL], for all designates States except US;
                       AGUR, Zvia, Tuval St, 11, 52522 Ramat-Gan, IL [IL, IL],
                       for US only;
                       ARAKELYAN, Levon, Tuval St, 11, 52522 Ramat-Gan, IL
                        [IL, IL], for US only;
                       VAINSTEIN, Vladimir, Tuval St, 11, 52522 Ramat-Gan, IL
                        [IL, IL], for US only
AGENT:
                       OPTIMATA LTD.$, c/o MANDIR, William, H., Sughrue Mion,
                       PLLC, 2100 Pennsylvania Ave., NW, Suite 800,
                       Washington, DC 20073-3213$, US
LANGUAGE OF FILING:
                       English
LANGUAGE OF PUBL :
                       English
DOCUMENT TYPE:
                       Patent
PATENT INFORMATION:
                       NUMBER
                                         KIND DATE
                       WO 2003036410 A2 20030501
DESIGNATED STATES
                       AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
      W:
                       CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
                       IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
                       MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI
                       SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
      RW (ARIPO):
                       GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
                       AM AZ BY KG KZ MD RU TJ TM
      RW (EAPO):
                      AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC
      RW (EPO):
```

MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW NL PT SE SK TR

RW (OAPI): BF BJ CF CG CI CM GA GN GO GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-IB4725 A 20021024 PRIORITY INFO.: US 2001-60/330,592 20011025 US 2002-10/207,772 20020731

A computer-implemented method for determining an optimal treatment ABEN protocol for a disease related to angiogenesis, comprising creating an angiogenesis model including pro-angiogenesis and anti-angiogenesis factors. Effective vessel density (EVD) is incorporated as a factor regulating switching on and switching off of at least one component in the angiogenesis model. Effects of vasculature maturation and mature vessels destabilization are incorporated. Pro-angiogenesis and anti-angiogenesis factors, which can influence changes in state of a tissue are selected. Effects of drugs in the pro-angiogenesis and anti-angiogenesis factors are incorporated. A plurality of treatment protocols in a protocol space is generated. A best treatment protocol based on a pre-determined criteria.

ABFR L'invention concerne un procede mis en oeuvre par ordinateur pour determiner un protocole de traitement optimal d'une maladie associee a l'angiogenese, qui consiste a creer un modele angiogenique comprenant des facteurs pro-angiogenese et des facteurs anti-angiogenese. Une densite effective des vaisseaux (EVD) est prise en compte en tant que facteur regulant la mise en service ou hors service d'au moins un element du modele angiogenique. Des effets de maturation du systeme vasculaire et de destabilisation des vaisseaux matures sont pris en compte. Des facteurs pro-angiogenese et des facteurs anti-angiogenese sont choisis, qui peuvent influer sur les changements d'etat d'un tissu. Les effets de medicaments sur les facteurs pro-angiogenese et les facteurs anti-angiogenese sont pris en compte. Plusieurs protocoles de traitement sont crees dans un espace de protocole. Un meilleur protocole de traitement est choisi sur la base de criteres preetablis.

ANSWER 9 OF 17 PCTFULL COPYRIGHT 2004 Univentio on STN 2002083851 PCTFULL ED 20021107 EW 200243 ACCESSION NUMBER:

TITLE (ENGLISH): VEGF FUSION PROTEINS TITLE (FRENCH): PROTEINES DE FUSION VEGF

KOVESDI, Imre, 7713 Warbler Lane, Rockville, MD 20855, INVENTOR(S):

US [US, US];

KESSLER, Paul, D., 1716 Algonquin Road, Frederick, MD

21701, US [US, US]

GENVEC, INC., 65 West Watkins Mill Road, Gaithersburg, MD 20878, US [US, US], for all designates States except PATENT ASSIGNEE(S):

KOVESDI, Imre, 7713 Warbler Lane, Rockville, MD 20855,

US [US, US], for US only;

KESSLER, Paul, D., 1716 Algonquin Road, Frederick, MD

21701, US [US, US], for US only

SMITH, Len, S.\$, Leydig, Voit & Mayer, Ltd., Suite

4900, Two Prudential Plaza, 180 North Stetson, Chicago,

IL 60601-6780\$, US

LANGUAGE OF FILING: LANGUAGE OF PUBL.:

English English Patent

DOCUMENT TYPE: PATENT INFORMATION:

KIND DATE NUMBER \_\_\_\_\_\_ WO 2002083851 A2 20021024

DESIGNATED STATES W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD

Page 8

AGENT:

MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW RW (ARIPO):

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-US11406 A 20020410 PRIORITY INFO.: US 2001-09/832,355 20010410

The invention provides therapeutic fusion proteins which include a first peptide portion comprising a first non-heparin binding VEGF peptide portion and a second non-VEGF peptide portion covalently associated with the first peptide portion, which first and second peptide portions separately promote angiogenesesis, bone growth, wound healing, or any combination thereof. Further provided are polynucleotides, encoding such fusion proteins, vectors including such polynucleotides, methods of making such proteins, and methods of promoting angiogenesis, bone growth, and/or wound healing using such proteins, polynucleotides, and

L'invention concerne des proteines de fusion therapeutiques comprenant ABFR une premiere partie peptidique renfermant une premiere partie de peptide VEGF de liaison non heparinique et une seconde partie de peptide non VEGF associee par covalence a la premiere partie de peptide, lesdites premiere et seconde parties de peptide favorisant separement l'angiogenese, la croissance osseuse, la cicatrisation des blessures ou toute combinaison associee. L'invention concerne en outre des polynucleotides codant pour ces proteines de fusion, des vecteurs comprenant ces polynucleotides, des methodes de fabrication de ces proteines ainsi que des methodes destinees a favoriser l'angiogenese, la croissance osseuse et/ou la cicatrisation des blessures au moyen de ces proteines, ces polynucleotides et ces vecteurs.

ANSWER 10 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2001:338563 CAPLUS

DOCUMENT NUMBER: 134:348629

TITLE: Modulation of eNOS activity using VEGF, a variant, or

VEGF receptor agonists and therapeutic uses thereof

INVENTOR(S): Shen, Ben-Quan; Zioncheck, Thomas

Genentech, Inc., USA PATENT ASSIGNEE(S): SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO. DATE
WO 2001032695	A2 20010510	WO 2000-US30294 20001102
WO 2001032695	A3 20020214	
W: AE, AG,	AL, AM, AT, AU,	AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU,	CZ, DE, DK, DM,	DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID,	IL, IN, IS, JP,	KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV,	MA, MD, MG, MK,	MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE,	SG, SI, SK, SL,	TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA,	ZW, AM, AZ, BY,	KG, KZ, MD, RU, TJ, TM
RW: GH, GM,	KE, LS, MW, MZ,	SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK,	ES, FI, FR, GB,	GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF,	CG, CI, CM, GA,	GN, GW, ML, MR, NE, SN, TD, TG
EP 1225910	A2 20020731	EP 2000-980281 20001102
R: AT, BE,	CH, DE, DK, ES,	FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2003513105 T220030408 JP 2001-535394 20001102

US 1999-163132P P 19991102 WO 2000-US30294 W 20001102 PRIORITY APPLN. INFO.:

AB The present invention provides uses of VEGF, a variant, or VEGF receptor agonists for the up-regulation of eNOS expression and activity. VEGF, its variants, and VEGF receptor agonists are useful in the treatment of or prevention from hypertension, diabetes, angina, thrombosis, atherosclerosis, heart failure, and other conditions or disorders wherein nitric oxide is an important regulator. Methods of preparing the variants are also disclosed in the patent.

ANSWER 11 OF 17 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

2001:378043 SCISEARCH ACCESSION NUMBER:

THE GENUINE ARTICLE: 428WH

TITLE: Vascular endothelial growth factor KDR receptor signaling

potentiates tumor necrosis factor-induced tissue factor

expression in endothelial cells

AUTHOR: Shen B Q; Lee D Y; Cortopassi K M; Damico L A; Zioncheck T

F (Reprint)

CORPORATE SOURCE: Genentech Inc, Dept Metab & Pharmacokinet, MS 70, 1 DNA

> Way, S San Francisco, CA 94080 USA (Reprint); Genentech Inc, Dept Metab & Pharmacokinet, S San Francisco, CA 94080

USA

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (16 FEB 2001) Vol. 276,

No. 7, pp. 5281-5286.

Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC,

9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.

ISSN: 0021-9258.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT:

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\* Vascular endothelial growth factor (VEGF) and tumor necrosis AB factor-alpha (TNF-alpha) have been shown to synergistically increase tissue factor (TF) expression in endothelial cells; however, the role of the VEGF receptors (KDR, Flt-1, and neuropilin) in this process is unclear. Here we report that VEGF binding to the KDR receptor is necessary and sufficient for the potentiation of TNF-induced TF expression in human umbilical vein endothelial cells. TF expression was evaluated by Western blot analysis and fluorescenceactivated cell sorting. In the absence of TNF-alpha, wild-type VEGF- or KDR receptor-selective variants induced an approximate 7-fold increase in total TF expression. Treatment with TNF alone produced an approximate 110-fold increase in total TF expression, whereas coincubation of TNF-alpha with wild-type VEGF- or KDR-selective variants resulted in an approximate 250-fold increase in TF expression. VEGF lacking the heparin binding domain was also able to potentiate TF expression, indicating that heparin-sulfate proteoglycan or neuropilin binding is not required for TF up-regulation. Neither placental growth factor nor an Flt-1-selective variant was capable of inducing TF expression in the presence or absence of TNF, Inhibition of protein-tyrosine kinase or protein kinase C activity significantly blocked the TNF/VEGF potentiation of TF up-regulation, whereas phorbol 12-myristate 13-acetate, a protein kinase C activator, increased TF expression. These data demonstrate that KDR receptor signaling governs both VEGF-induced TF expression and the potentiation of TNF-induced up-regulation of TF.

ANSWER 12 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

1.5

09/700806 14/06/2004 ACCESSION NUMBER: 2000:756863 CAPLUS DOCUMENT NUMBER: 133:318304 TITLE: Vascular endothelial cell growth factor (VEGF) variants and pharmaceutical uses thereof INVENTOR(S): Cunningham, Brian; Abraham, Devos; Li, Bing Genentech, Inc., USA PATENT ASSIGNEE(S): SOURCE: PCT Int. Appl., 70 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent English LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE WO 2000063380 A1 20001026 WO 2000-US9483 20000410 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG A1 20020116 EP 2000-921966 EP 1171594 20000410 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO JP 2002541849 T220021210 JP 2000-612459 20000410 NZ 2000-514488 NZ 514488 Α 20040130 20000410 AU 771042 B2 20040311 AU 2000-42220 20000410 PRIORITY APPLN. INFO.: US 1999-129788P P 19990416 US 2000-184235P P 20000223 WO 2000-US9483 W 20000410 AΒ The present invention provides VEGF variants having at least a single amino acid mutation in the native VEGF sequence and selective binding affinity for either the kinase domain region ( KDR) receptor or the FMS-like tyrosine kinase region (FLT-1) receptor. Methods of making the VEGF variants and methods of using the VEGF variants are also provided. The VEGF variants may have pharmaceutical applications. Only sequence #1, 2, 7, 8 are claimed. THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 3 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT ANSWER 13 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3 1.5 2000:716110 CAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 133:291561 TITLE: Vascular endothelial growth factor C (VEGF-C) ACys156 protein and gene, and uses thereof INVENTOR(S): Alitalo, Kari; Joukov, Vladimir Helsinki University Licensing, Ltd., Finland PATENT ASSIGNEE(S): SOURCE: U.S., 87 pp. CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 12

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6130071	А	20001010	US 1997-795430	19970205

```
A1 19980806
    WO 9833917
                                        WO 1998-US1973
        W: AU, CA, CN, JP, NZ, US, US, US, US, US, US, US, RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
                                       AU 1998-62624
    AU 9862624 A1 19980825
                                                          19980202
    AU 748369
                     B2
                           20020606
    EP 972028
                     A1
                           20000119
                                        EP 1998-904842 19980202
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
    JP 2001523951
                     T2 20011127
                                         JP 1998-533178
                                                          19980202
    US 6361946
                    B1 20020326
                                        US 1999-355700
                                                          19991105
                     B2 20021219
                                         AU 2000-10072
                                                          20000113
    AU 755708
    US 2003091567 A1 20030515
                                         US 2002-201386
                                                          20020723
                                      US 1994-340011 A2 19941114
PRIORITY APPLN. INFO.:
                                      US 1995-510133 A2 19950801
                                       US 1996-585895 A2 19960112
                                       US 1996-601132 A2 19960214
                                       US 1996-671573 A2 19960628
                                       AU 1996-66169 A3 19960801
                                       WO 1996-FI427 A2 19960801
                                       US 1997-795430 A2 19970205
                                       WO 1998-US1973 W 19980202
                                       US 1999-355700 A1 19991105
                                       US 2000-534376 A1 20000324
    Provided are purified and isolated VEGF-C cysteine deletion
AΒ
    variants that bind to Flt4 receptor tyrosine kinase (VEGFR-3) but
    demonstrate reduced binding (relative to VEGF-C) to kdr
    receptor tyrosine kinase (VEGFR-2); polynucleotides encoding the
    polypeptide; vectors and host cells that embody the polynucleotides;
    pharmaceutical compns. and diagnostic reagents comprising the
    polypeptides; and methods of making and using the foregoing. The variants
    are expected to have the same biol. activities as VEGF-C (including but
    not limited to affecting growth and migration of vascular endothelial
    cells; promoting growth of lymphatic endothelial cells and lymphatic
    vessels; increasing vascular permeability; and affecting myelopoiesis )
     support numerous diagnostic and in vitro and in vivo clin. utilities for
    polypeptides and antibodies of the invention, for modulating (stimulating
    or inhibiting) these biol. activities.
                        210
                              THERE ARE 210 CITED REFERENCES AVAILABLE FOR
REFERENCE COUNT:
                              THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
                              FORMAT
    ANSWER 14 OF 17 USPATFULL on STN
L_5
                       2000:54211 USPATFULL
ACCESSION NUMBER:
                       Variants of vascular endothelial cell growth factor
TITLE:
                       Keyt, Bruce A., Pacifica, CA, United States
INVENTOR(S):
                       Nguyen, Francis Hung, Daly City, CA, United States
                       Ferrara, Napoleone, San Francisco, CA, United States
                       Cunningham, Brian C., San Mateo, CA, United States
                       Wells, James A., Burlingame, CA, United States
                       Li, Bing, Foster City, CA, United States
                       Genentech, Inc., S. San Francisco, CA, United States
PATENT ASSIGNEE(S):
                       (U.S. corporation)
                           NUMBER
                                       KIND DATE
                       -----
                       US 6057428 20000502
US 1996-691794 19960802
PATENT INFORMATION:
APPLICATION INFO.:
                                                        (8)
                       Continuation of Ser. No. US 1995-567200, filed on 5 Dec
RELATED APPLN. INFO.:
                       1995
DOCUMENT TYPE:
                       Utility
```

FILE SEGMENT:

Granted

ASSISTANT EXAMINER: Feisee, Lila NUMBER OF CLAIMS. Kaufman, Claims

Kaufman, Claire M.

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 27 Drawing Figure(s); 24 Drawing Page(s) LINE COUNT: 3120

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention involves the preparation of vascular endothelial growth factor (VEGF) variants which provide materials that are selective in respect to binding characteristics to the kinase domain region and the FMS-like tyrosine-kinase region, respectively KDR and FLT-1. The respective KDR and FLT-1 receptors are bound by corresponding domains within the VEGF compound domains. The variants hereof define those two binding regions and modify them so as to introduce changes that interrupt the binding to the respective domain. In this fashion the final biological characteristics of the VEGF molecule are selectively modified.

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 15 OF 17 USPATFULL on STN

ACCESSION NUMBER:

2000:12936 USPATFULL

Nucleic acids encoding variants of vascular endothelial

cell growth factor

INVENTOR (S):

Keyt, Bruce A., Pacifica, CA, United States

Nguyen, Francis Hung, Daly City, CA, United States Ferrara, Napoleone, San Francisco, CA, United States Genentech, Inc., S. San Francisco, CA, United States

(U.S. corporation)

NUMBER KIND DATE -----

PATENT ASSIGNEE(S):

PATENT INFORMATION: US 6020473 20000201
APPLICATION INFO.: US 1995-567200 19951205 (8)
DOCUMENT TYPE: Utility

Granted

DOCUMENT TYPE: FILE SEGMENT:

PRIMARY EXAMINER: Spector, Lorraine
ASSISTANT EXAMINER: Kaufman, Claire M.
LEGAL REPRESENTATIVE: Johnston, Sean, Vance, Dolly A.Flehr Hohbach Test

Albritton & Herbert LLP

Albritton & Herbert LLP

NUMBER OF CLAIMS: 8

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 23 Drawing Figure(s); 21 Drawing Page(s)

LINE COUNT: 2668

LINE COUNT:

2668

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention involves the preparation of vascular endothelial growth factor (VEGF) variants which provide materials that are selective in respect to binding characteristics to the kinase domain region and the FMS-like tyrosine-kinase region, respectively KDR and FLT-1. The respective KDR and FLT-1 receptors are bound by corresponding domains within the VEGF compound domains. The variants hereof define those two binding regions and modify them so as to introduce changes that interrupt the binding to the respective domain. In this fashion the final biological characteristics of the VEGF molecule are selectively modified.

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 16 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:696070 CAPLUS DOCUMENT NUMBER: 133:305707

TITLE: Receptor-selective variants of human vascular

endothelial growth factor: generation and

characterization

Li, Bing; Fuh, Germaine; Meng, Gloria; Xin, Xiaohua; AUTHOR (S):

Gerritsen, Mary E.; Cunningham, Brian; De Vos, Abraham

Department of Protein Engineering, Genentech, Inc., CORPORATE SOURCE:

South San Francisco, CA, 94080, USA

Journal of Biological Chemistry (2000), 275(38), SOURCE:

29823-29828

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular

Biology

DOCUMENT TYPE:

Journal

LANGUAGE: English

Vascular endothelial growth factor (VEGF) is a pleiotropic factor that exerts a multitude of biol. effects through its interaction with two receptor tyrosine kinases, fms-like tyrosine kinase (Flt-1) or VEGF receptor 1 and kinase insert domain-containing receptor (KDR) or VEGF receptor 2. Whereas it is commonly accepted that KDR is responsible for the proliferative activities of VEGF, considerable controversy and uncertainty exist about the role of the individual receptors in eliciting many of the other effects. Based on a comprehensive mutational anal. of the receptor-binding site of VEGF, an Flt-1-selective variant was created containing four substitutions from the wild-type protein. This variant bound with wild-type affinity to Flt-1, was at least 470-fold reduced in binding to KDR, and had no activity in cell-based assays measuring autophosphorylation of KDR or proliferation of primary human vascular endothelial cells. Using a competitive phage display strategy, two KDR-selective variants were discovered with three and four changes from wild-type, resp. Both variants had approx. wild-type affinity for KDR, were about 2000-fold reduced in binding to Flt-1, and showed activity comparable with the wild-type protein in KDR autophosphorylation and endothelial cell proliferation assays. These variants will serve as

useful reagents in elucidating the roles of Flt-1 and KDR.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 17 OF 17 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 1998016551 PCTFULL ED 20020514

TITLE (ENGLISH): VARIANTS OF VASCULAR ENDOTHELIAL CELL GROWTH FACTOR

HAVING ANTAGONISTIC PROPERTIES

TITLE (FRENCH): VARIANTS DE FACTEUR DE CROISSANCE DE CELLULES

ENDOTHELIALES VASCULAIRES POSSEDANT DES PROPRIETES

ANTAGONISTES

INVENTOR(S): KEYT, Bruce, A.;

> NGUYEN, Francis, Hung; FERRARA, Napoleone

GENENTECH, INC.; PATENT ASSIGNEE(S):

KEYT, Bruce, A.;

NGUYEN, Francis, Hung; FERRARA, Napoleone

LANGUAGE OF PUBL.:

English

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

NUMBER KIND DATE ------WO 9816551 A2 19980423

DESIGNATED STATES

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE W :

ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR

```
LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE
                        SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH KE LS
                        MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE
                        DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI
                        CM GA GN ML MR NE SN TD TG
APPLICATION INFO.:
                        WO 1997-US19471
                                             A 19971010
PRIORITY INFO.:
                        US 1996-8/734,443
                                                19961017
ABEN
       The present invention involves the preparation of vascular endothelial
       growth factor (VEGF)
       antagonist molecules comprising variant VEGF polypeptides which are
       capable of binding to and
       occuyping cell surface VEGF receptors without inducing a VEGF response,
       thereby antagonizing the
       biological activity of the native VEGF protein. Specifically, the
       variant VEGF polypeptides of the
       present invention comprise modifications of at least one cysteine
       residue in the native VEGF
       sequence, thereby inhibiting the ability of the variant polypeptide to
       dimerize through the
       formation of disulfide bonds. The present invention is further directed
       to methods for preparing
       such variant VEGF antagonists and to methods, compositions and assays
       utilizing such variants for
       producing pharmaceutically active materials having therapeutic and
       pharmacologic properties that
       differ from the native VEGF protein.
ABFR
       L'invention concerne la preparation de molecules antagonistes du facteur
       de croissance
       endotheliale vasculaire (VEGF) comprenant des variants de polypeptides
       de VEGF capables de se lier
       aux recepteurs de VEGF a la surface des cellules et de les occuper sans
       produire une reponse VEGF,
       ayant ainsi un effet antagoniste sur l'activite biologique de la
       proteine de VEGF native. En
       particulier, les variants de polypeptides de VEGF faisant l'objet de la
       presente invention
       comprennent des modifications d'au moins un residu de cysteine dans la
       sequence de VEGF native,
       inhibant ainsi la capacite du variant de polypeptide a dimeriser par
       formation de ponts disulfures.
       La presente invention prevoir eqalement des procedes de preparation de
       tels variants d'antagonistes
       du VEGF ainsi que des procedes, des compositions et des analyses pour
       lesquels on utilise de tels
       variants en vue de produire des matieres pharmaceutiquement actives
       possedant des proprietes
       therapeutiques et pharmacologiques qui different de la proteine de VEGF
       native.
=> d his
     (FILE 'HOME' ENTERED AT 13:38:21 ON 14 JUN 2004)
     FILE 'MEDLINE, CAPLUS, SCISEARCH, BIOSIS, USPATFULL, PCTFULL' ENTERED AT
     13:38:43 ON 14 JUN 2004
L1
            880 S KDR (W) RECEPTOR?
L2
            11 S VEGF(W) RECEPTOR(W) AGONIST?
L3
            777 S VEGF (3A) VARIANT?
L4
            21 S L1(S)(L2 OR L3)
            17 DUP REM L4 (4 DUPLICATES REMOVED)
L5
```

```
=> s amino(w)acid(w) (substitution? or change? or convert? or mutated or mutation) (w) vegf
   2 FILES SEARCHED...
   5 FILES SEARCHED...
          230 AMINO(W) ACID(W) (SUBSTITUTION? OR CHANGE? OR CONVERT? OR MUTATED
               OR MUTATION) (W) VEGF
=> s (d63s or g65m or 166r or asp63 or d63 or gly65 or g65 or leu66 or 166)(s)vegf
L66 NOT FOUND
The L-number entered could not be found. To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).
=> s (d63s or g65m or 166r or asp63 or d63 or gly65 or g65 or leu66)(s)vegf
           29 (D63S OR G65M OR L66R OR ASP63 OR D63 OR GLY65 OR G65 OR LEU66) (
L7
              S) VEGF
=> dup rem 17
PROCESSING COMPLETED FOR L7
            27 DUP REM L7 (2 DUPLICATES REMOVED)
=> d his
     (FILE 'HOME' ENTERED AT 13:38:21 ON 14 JUN 2004)
    FILE 'MEDLINE, CAPLUS, SCISEARCH, BIOSIS, USPATFULL, PCTFULL' ENTERED AT
    13:38:43 ON 14 JUN 2004
L1
           880 S KDR (W) RECEPTOR?
           11 S VEGF(W) RECEPTOR (W) AGONIST?
L2
           777 S VEGF (3A) VARIANT?
L3
            21 S L1(S)(L2 OR L3)
L4
            17 DUP REM L4 (4 DUPLICATES REMOVED)
L5
           230 S AMINO(W) ACID(W) (SUBSTITUTION? OR CHANGE? OR CONVERT? OR MUTAT
L6
            29 S (D63S OR G65M OR L66R OR ASP63 OR D63 OR GLY65 OR G65 OR LEU6
L7
            27 DUP REM L7 (2 DUPLICATES REMOVED)
T.8
=> s 18 and 16 and 11
           0 L8 AND L6 AND L1
L9
=> s 18 and 11
    16 L8 AND L1
L10
=> d ibib abs 1-16
L10 ANSWER 1 OF 16 USPATFULL on STN
                       2004:88227 USPATFULL
ACCESSION NUMBER:
TITLE:
                       Targeted therapeutic lipid constructs
INVENTOR(S):
                       Brunke, Karen J., Belmont, CA, UNITED STATES
                       Wartchow, Charles A., San Francisco, CA, UNITED STATES
                       Cleland, Jeffrey L., San Carlos, CA, UNITED STATES
                                     KIND DATE
                           NUMBER
                       ______
PATENT INFORMATION: US 2004067196 A1 20040408 APPLICATION INFO.: US 2003-401280 A1 20030327 (10)
RELATED APPLN. INFO.:
                       Continuation-in-part of Ser. No. US 2001-976254, filed
                       on 11 Oct 2001, PENDING
                              NUMBER DATE
                       _____
```

US 2000-239684P 20001011 (60)

US 2002-367858P 20020327 (60)

PRIORITY INFORMATION:

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE: SWANSON & BRATSCHUN L.L.C., 1745 SHEA CENTER DRIVE,

SUITE 330, HIGHLANDS RANCH, CO. 80129

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 2 Drawing Page(s)

LINE COUNT: 2334

CAS INDEXING IS AVAILABLE FOR THIS PATENT. Novel therapeutic lipid constructs comprising a lipid construct, an

anti-cell surface targeting agent, and a radiotherapeutic metal ion are

disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 2 OF 16 USPATFULL on STN

ACCESSION NUMBER:

2004:44956 USPATFULL

TITLE:

Use of VEGF for treating bone defects

INVENTOR (S):

Bunting, Stuart, Half Moon Bay, CA, UNITED STATES

Carano, Richard, San Ramon, CA, UNITED STATES

Filvaroff, Ellen Hope, San Francisco, CA, UNITED STATES Gosselin, Richard Andre, El Granada, CA, UNITED STATES Peale, Franklin V., JR., San Carlos, CA, UNITED STATES

PATENT ASSIGNEE(S):

GENENTECH, INC. (U.S. corporation)

NUMBER KIND DATE \_\_\_\_\_\_

PATENT INFORMATION: US 2004033949 A1 20040219 APPLICATION INFO.: US 2003-431105 A1 20030506 (10)

NUMBER DATE \_\_\_\_\_\_

PRIORITY INFORMATION: US 2002-378275P 20020506 (60)

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE: GENENTECH, INC., 1 DNA WAY, SOUTH SAN FRANCISCO, CA,

94080

NUMBER OF CLAIMS:

31

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS:

7 Drawing Page(s)

LINE COUNT:

1650

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides pharmaceutical compositions comprising VEGF or variants thereof for promoting bone formation, in vitro and in vivo. Methods of using those compositions are also provided.

Compositions and methods of the present invention can be used for promoting and improving the repair process in subjects with bone

defects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 3 OF 16 USPATFULL on STN

ACCESSION NUMBER:

2003:119619 USPATFULL

TITLE:

Targeted therapeutic lipid constructs having cell

surface targets

INVENTOR(S):

Wartchow, Charles Aaron, San Carlos, CA, UNITED STATES

Pease, John S., Los Altos, CA, UNITED STATES Shen, Zhi Min, Palo Alto, CA, UNITED STATES

PATENT ASSIGNEE(S):

TARGESOME, INC. (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 2003082103 A1 20030501 APPLICATION INFO.: US 2002-262576 A1 20021001 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-976254, filed

on 11 Oct 2001, PENDING

NUMBER DATE

-----US 2000-239684P 20001011 (60) PRIORITY INFORMATION:

US 2001-326310P 20011001 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: SWANSON & BRATSCHUN L.L.C., 1745 SHEA CENTER DRIVE,

SUITE 330, HIGHLANDS RANCH, CO, 80129

NUMBER OF CLAIMS:

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 2 Drawing Page(s)

LINE COUNT: 2294

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Novel therapeutic lipid constructs comprising a polymerized liposome, an anti-cell surface targeting agent, and a radiotherapeutic metal ion are

disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 4 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2002:112878 USPATFULL

Ligand for vascular endothelial growth factor receptor TITLE:

INVENTOR(S): Tchistiakova, Lioudmila, Laval, CANADA

Li, Shengmin, Laval, CANADA

Pietrzynski, Grzegorz, Montreal, CANADA Alakhov, Valery, Baie d'Urfe, CANADA

NUMBER KIND DATE -----US 2002058619 A1 20020516 US 6733755 B2 20040511 US 2001-775743 A1 20010202 (9) PATENT INFORMATION: APPLICATION INFO.:

NUMBER DATE

-----PRIORITY INFORMATION: US 2000-180568P 20000204 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: GIBBONS, DEL DEO, DOLAN, GRIFFINGER & VECCHIONE, 1

RIVERFRONT PLAZA, NEWARK, NJ, 07102-5497

NUMBER OF CLAIMS: 24 EXEMPLARY CLAIM: 1 LINE COUNT: 3407

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to compositions comprised of a peptide ligand or derivatives thereof that are capable of specific binding to the high affinity receptor-1 of vascular endothelial growth factor (VEGF) and structure similar receptors. The invention further provides a peptide ligand or derivatives thereof that are capable of inhibiting angiogenesis induced by VEGF. The present invention also provides a method for treatment or diagnosis of disease associated with angiogenesis in a patient in need of therapy comprising administering to the patient an effective amount of the pharmaceutical composition of the present invention and a pharmaceutical acceptable carrier.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 5 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2000:54211 USPATFULL

TITLE: Variants of vascular endothelial cell growth factor

INVENTOR(S): Keyt, Bruce A., Pacifica, CA, United States

> Nguyen, Francis Hung, Daly City, CA, United States Ferrara, Napoleone, San Francisco, CA, United States Cunningham, Brian C., San Mateo, CA, United States Wells, James A., Burlingame, CA, United States

Li, Bing, Foster City, CA, United States

PATENT ASSIGNEE(S): Genentech, Inc., S. San Francisco, CA, United States

(U.S. corporation)

NUMBER KIND DATE -----

PATENT INFORMATION: US 6057428 20000502 APPLICATION INFO.: US 1996-691794 19960802 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-567200, filed on 5 Dec

1995

DOCUMENT TYPE: Utility Granted FILE SEGMENT:
PRIMARY EXAMINER:
ASSISTANT EXAMINER:
Kaufman, Claire M. FILE SEGMENT:

ASSISTANI BALL. NUMBER OF CLAIMS: 20

NUMBER OF DRAWINGS: 27 Drawing Figure(s); 24 Drawing Page(s) LINE COUNT: 3120

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention involves the preparation of vascular endothelial AB growth factor (VEGF) variants which provide materials that are selective in respect to binding characteristics to the kinase domain region and the FMS-like tyrosine-kinase region, respectively KDR and FLT-1. The respective KDR and FLT-1 receptors are bound by corresponding domains within the VEGF compound domains. The variants hereof define those two binding regions and modify them so as to introduce changes that interrupt the binding to the respective domain. In this fashion the final biological characteristics of the VEGF molecule are selectively modified.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 6 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2000:12936 USPATFULL

TITLE: Nucleic acids encoding variants of vascular endothelial

cell growth factor

INVENTOR(S): Keyt, Bruce A., Pacifica, CA, United States

Nguyen, Francis Hung, Daly City, CA, United States Ferrara, Napoleone, San Francisco, CA, United States

Genentech, Inc., S. San Francisco, CA, United States

(U.S. corporation)

NUMBER KIND DATE -----20000201

PATENT INFORMATION: US 6020473
APPLICATION INFO.: US 1995-567200 19951205 (8)

DOCUMENT TYPE: Utility

PATENT ASSIGNEE(S):

FILE SEGMENT: Granted
PRIMARY EXAMINER: Spector, Lorraine
ASSISTANT EXAMINER: Kaufman, Claire M.

LEGAL REPRESENTATIVE: Johnston, Sean, Vance, Dolly A.Flehr Hohbach Test

Albritton & Herbert LLP

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 23 Drawing Figure(s); 21 Drawing Page(s)

LINE COUNT: 2668

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

1

The present invention involves the preparation of vascular endothelial growth factor (VEGF) variants which provide materials that are selective in respect to binding characteristics to the kinase domain region and the FMS-like tyrosine-kinase region, respectively KDR and FLT-1. The respective KDR and FLT-1 receptors are bound by corresponding domains within the VEGF compound domains. The variants hereof define those two binding regions and modify them so as to introduce changes that interrupt the binding to the respective domain. In this fashion the final biological characteristics of the VEGF molecule are selectively modified.

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 7 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2003094617 PCTFULL ED 20031125 EW 200347
TITLE (ENGLISH): USE OF VEGF FOR TREATING BONE DEFECTS
TITLE (FRENCH): UTILISATION DE VEGF POUR TRAITER DES DEFAUTS OSSEUX

TITLE (FRENCH): UTILISATION DE VEGF POUR TRAITER DES DEFAUTS OSSEUX INVENTOR(S): BUNTING, Stuart, 220 Miramontes Avenue, Half Moon Bay,

CA 94019, US;

FILVAROFF, Ellen Hope, 538 18th Avenue, San Francisco,

CA 94121, US;

PEALE, Jr., Franklin V., 416 Pearl Avenue, San Carlos,

CA 94070, US;

CARANO, Richard, 2470 Paddock Drive, San Ramon, CA

94583, US;

GOSSELIN, Richard Andre, 643 Ferdinand Avenue, El

Granada, CA 94018, US

PATENT ASSIGNEE(S): GENENTECH, INC., 1 DNA Way, South San Francisco, CA

94080-4990, US [US, US]

AGENT: CUI, Steven X.\$, GENENTECH, INC., 1 DNA Way, South San

Francisco, CA 94080-4990\$, US

LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE

WO 2003094617 A2 20031120

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR

CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE

SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU

MC NL PT RO SE SI SK TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2003-US14090 A 20030506 PRIORITY INFO.: US 2002-60/378,275 20020506

ABEN The present invention provides pharmaceutical compositions comprising VEGF or variants thereof for promoting bone formation, <i>in vitro</i> and <i>in vivo</i>. Methods of using those compositions are also

provided. Compositions and methods of the present invention can be used

for promoting and improving the repair process in subjects with bone defects.

ABFR

L'invention concerne des compositions pharmaceutiques comprenant VEGF ou ses variants, lesquelles compositions permettant de favoriser la formation osseuse, <i>in vitro</i> et <i>in vivo</i>. L'invention concerne des methodes d'utilisation de ces compositions. Les compositions et les methodes de l'invention peuvent etre utilisees pour favoriser et pour ameliorer le processus de reparation chez des sujets presentant des defauts osseux.

L10 ANSWER 8 OF 16 PCTFULL ACCESSION NUMBER:

COPYRIGHT 2004 Univentio on STN 2002083851 PCTFULL ED 20021107 EW 200243

TITLE (ENGLISH): TITLE (FRENCH): INVENTOR(S):

VEGF FUSION PROTEINS PROTEINES DE FUSION VEGF

KOVESDI, Imre, 7713 Warbler Lane, Rockville, MD 20855,

US [US, US];

KESSLER, Paul, D., 1716 Algonquin Road, Frederick, MD

21701, US [US, US]

PATENT ASSIGNEE(S):

GENVEC, INC., 65 West Watkins Mill Road, Gaithersburg, MD 20878, US [US, US], for all designates States except

KOVESDI, Imre, 7713 Warbler Lane, Rockville, MD 20855,

US [US, US], for US only;

KESSLER, Paul, D., 1716 Algonquin Road, Frederick, MD

21701, US [US, US], for US only

AGENT:

SMITH, Len, S.\$, Leydig, Voit & Mayer, Ltd., Suite 4900, Two Prudential Plaza, 180 North Stetson, Chicago,

IL 60601-6780\$, US

LANGUAGE OF FILING: LANGUAGE OF PUBL.:

English English Patent

PATENT INFORMATION:

DOCUMENT TYPE:

KIND DATE NUMBER \_\_\_\_\_ WO 2002083851 A2 20021024

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

RW (ARIPO):

GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO):

AM AZ BY KG KZ MD RU TJ TM

RW (EPO):

AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG APPLICATION INFO.: WO 2002-US11406 A 20020410 PRIORITY INFO.: US 2001-09/832,355 20010410

US 2001-09/832,355

20010410

PRIORITY INFO.: ABEN

The invention provides therapeutic fusion proteins which include a first peptide portion comprising a first non-heparin binding VEGF peptide portion and a second non-VEGF peptide portion covalently associated with the first peptide portion, which first and second peptide portions separately promote angiogenesesis, bone growth, wound healing, or any combination thereof. Further provided are polynucleotides, encoding such fusion proteins, vectors including such polynucleotides, methods of making such proteins, and methods of promoting angiogenesis, bone growth, and/or wound healing using such proteins, polynucleotides, and

vectors.

L'invention concerne des proteines de fusion therapeutiques comprenant ABFR une premiere partie peptidique renfermant une premiere partie de peptide VEGF de liaison non heparinique et une seconde partie de peptide non

VEGF associee par covalence a la premiere partie de peptide, lesdites premiere et seconde parties de peptide favorisant separement l'angiogenese, la croissance osseuse, la cicatrisation des blessures ou toute combinaison associee. L'invention concerne en outre des polynucleotides codant pour ces proteines de fusion, des vecteurs comprenant ces polynucleotides, des methodes de fabrication de ces proteines ainsi que des methodes destinees a favoriser l'angiogenese, la croissance osseuse et/ou la cicatrisation des blessures au moyen de ces proteines, ces polynucleotides et ces vecteurs.

L10 ANSWER 9 OF 16 ACCESSION NUMBER: TITLE (ENGLISH): TITLE (FRENCH): INVENTOR(S):

PCTFULL COPYRIGHT 2004 Univentio on STN 2002081520 PCTFULL ED 20021028 EW 200242

SINGLE CHAIN DIMERIC POLYPEPTIDES POLYPEPTIDE DIMERIQUE A CHAINE SIMPLE

BOESEN, Thomas, Peter, Aksel Mollers Have 7, DK-2000

Frederiksberg, DK [DK, DK];

HALKIER, Torben, Lyngvej 5, DK-2680 Solrod Strand, DK

[DK, DK]

PATENT ASSIGNEE(S):

MAXYGEN HOLDINGS LTD., c/o Close Brothers (Cayman) Limited, 103 South Church Street, P.O. Box 1034 GT, Grand Cayman, KY [—, —], for all

designates States except US;

BOESEN, Thomas, Peter, Aksel Mollers Have 7, DK-2000

Frederiksberg, DK [DK, DK], for US only;

HALKIER, Torben, Lyngvej 5, DK-2680 Solrod Strand, DK

[DK, DK], for US only

MAXYGEN APS\$, Agern Alle 1, DK-2970 Horsholm\$, DK AGENT:

LANGUAGE OF FILING: LANGUAGE OF PUBL.: DOCUMENT TYPE: PATENT INFORMATION: English English Patent

NUMBER KIND DATE \_\_\_\_\_\_ WO 2002081520 A2 20021017

DESIGNATED STATES

W·

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

RW (ARIPO): RW (EAPO): RW (EPO):

AM AZ BY KG KZ MD RU TJ TM

AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

TR

RW (OAPI):

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: PRIORITY INFO.:

WO 2002-DK233 A 20020408 DK 2001-PA 2001 00578 20010406

GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

US 2001-60/282,239

20010406

AREN

The invention relates to a single-chain dimeric polypeptide which binds to an extracellular ligand-binding domain of a VEGF type 2 receptor (KDR) or a VEGF type 3 receptor (Flt-4), the polypeptide comprising two receptor-binding sites of which one is capable of binding to a ligand-binding domain of the receptor and one is incapable of effectively binding to a ligand-binding domain of the receptor, and wherein at least one monomer of the dimeric polypeptide is derived from VEGF, VEGF-C or VEGF-D, whereby the single-chain dimeric polypeptide is capable of binding to the receptor, but incapable of activating the receptor. The polypeptide functions as a receptor antagonist for prevention or treatment of a disease or condition involving increased signal transduction from or increased activation of the KDR and/or Flt-4 receptor, e.g. to inhibit angiogenesis or lymphangiogenesis.

ABFR L'invention concerne un polypeptide dimerique a chaine simple qui se lie a un domaine extracellulaire de liaison aux ligands d'un recepteur VEGF type 2 (KDR) ou d'un recepteur VEGF type 3 (Flt-4), le polypeptide contenant deux sites de liaison aux recepteurs, l'un pouvant se lier a un domaine de liaison aux ligands du recepteur et l'autre ne pouvant pas se lier efficacement a un domaine de liaison aux ligands du recepteur. Au moins un monomere du polypeptide dimerique est derive de VEGF, VEGF-C ou VEGF-D, le polypeptide dimerique a chaine simple pouvant se lier au recepteur mais ne pouvant pas activer le recepteur. Le polypeptide fonctionne comme un antagoniste de recepteur permettant de prevenir ou de traiter une maladie ou un etat impliquant une transduction accrue de signal du recepteur KDR et/ou Flt-4 ou une activation accrue dudit recepteur, notamment pour inhiber une angiogenese ou une lymphangiogenese.

ANSWER 10 OF 16 PCTFULL L10 COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 2001057067 PCTFULL ED 20020827

LIGAND FOR VASCULAR ENDOTHELIAL GROWTH FACTOR RECEPTOR TITLE (ENGLISH):

LIGAND DU RECEPTEUR DE FACTEUR DE CROISSANCE TITLE (FRENCH):

ENDOTHELIAL VASCULAIRE INVENTOR(S): TCHISTIAKOVA, Lioudmila;

LI, Shengmin:

PIETRZYNSKI, Grzegorz;

ALAKHOV, Valery

SUPRATEK PHARMA INC. PATENT ASSIGNEE(S):

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE \_\_\_\_\_\_ WO 2001057067 A1 20010809

DESIGNATED STATES

W·

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2001-IB135 US 2000-60/180,568 A 20010202

PRIORITY INFO.:

20000204

The present invention relates to compositions comprised of a peptide ABEN ligand or derivatives thereof that are capable of specific binding to the high affinity receptor-1 of vascular endothelial growth factor (VEGF) and structure similar receptors. The invention further provides a peptide ligand or derivatives thereof that are capable of inhibiting angiogenesis induced by VEGF. The present invention also provides a method for treatment or diagnosis of disease associated with angiogenesis in a patient in need of therapy comprising administering to the patient an effective amount of the pharmaceutical composition of the present invention and a pharmaceutical acceptable carrier.

ABFR

L'invention concerne des compositions contenant un ligand peptidique ou des derives de celui-ci qui sont capables de se lier specifiquement au recepteur 1 de grande affinite pour le facteur de croissance endothelial vasculaire (VEGF) et a des recepteurs a structure similaire. L'invention concerne de plus un liqand peptidique ou des derives de celui-ci qui sont capables d'inhiber l'angiogenese induite par VEGF. L'invention concerne aussi une methode permettant de traiter ou de diagnostiquer une maladie associee a l'angiogenese chez un patient necessitant un tel traitement; cette methode comprend l'administration au patient d'une quantite efficace de la composition pharmaceutique de l'invention et

d'un excipient pharmaceutiquement acceptable.

L10 ANSWER 11 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 2001032695 PCTFULL ED 20020820

TITLE (ENGLISH): MODULATION OF ENOS ACTIVITY AND THERAPEUTIC USES

TITLE (FRENCH):

MODULATION DE L'ACTIVITE DE L'ENOS ET SES UTILISATIONS SHEN, Ben-Quan;

INVENTOR(S):

ZIONCHECK, Thomas

PATENT ASSIGNEE(S): GENENTECH, INC.; SHEN, Ben-Quan; ZIONCHECK, Thomas

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

NUMBER KIND DATE WO 2001032695 A2 20010510

DESIGNATED STATES

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF

CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US30294 A 20001102 PRIORITY INFO.: US 1999-60/163,132 19991102

The present invention provides uses of VEGF or VEGF receptor agonists ABEN for the up-regulation of eNOS expression and activity. VEGF and VEGF receptor agonists are useful in the treatment of or prevention from hypertension, diabetes, angina, thrombosis, atherosclerosis, heart failure, and other conditions or disorders wherein nitric oxide is an important regulator.

ABFR

ANSWER 12 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN L10

ACCESSION NUMBER: 2001012809 PCTFULL ED 20020828

METHODS AND MEANS FOR INHIBITING ANGIOGENESIS
PROCEDES ET SYSTEMES POUR INHIBER L'ANGIOGENESE TITLE (ENGLISH): TITLE (FRENCH):

INVENTOR(S):

LEENDERS, Wilhelmus, Petrus, Johannes;

LUBSEN, Nicolette, Hermance;

DE WAAL, Robert, Marius, Walther

PATENT ASSIGNEE(S):

INTROGENE B.V.; LEENDERS, Wilhelmus, Petrus, Johannes;

LUBSEN, Nicolette, Hermance; DE WAAL, Robert, Marius, Walther

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

NUMBER KIND DATE \_\_\_\_\_\_ WO 2001012809 A2 20010222

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG

CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-NL570 A 20000814 PRIORITY INFO.: EP 1999-99202641.9 19990813

The present invention discloses heterodimeric VEGF variants with ABEN functional VEGF-receptor binding sites at one pole of the asymmetrical dimer, and mutations in the domains for binding to the VEGF tyrosine kinase receptors KDR and Flt-1 at the other pole. These molecules are potent inhibitors of VEGF-induced proliferation and tissue factor induction in endothelial cells and of vascular hyperpermeability.

ABFR

ANSWER 13 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN 1.10

ACCESSION NUMBER: 2001009157 PCTFULL ED 20020828

HIGH AFFINITY VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) TITLE (ENGLISH):

RECEPTOR NUCLEIC ACID LIGANDS AND INHIBITORS

LIGANDS ET INHIBITEURS ACIDE NUCLEIQUE DE RECEPTEUR A TITLE (FRENCH):

FACTEUR DE CROISSANCE A FORTE AFFINITE VASCULAIRE

ENDOTHELIALE (VEGF)

INVENTOR (S): JANJIC, Nebojsa;

GOLD, Larry

PATENT ASSIGNEE(S): NEXSTAR PHARMACEUTICALS, INC.;

JANJIC, Neboisa;

GOLD, Larry

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE WO 2001009157 A1 20010208

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US20478 A 20000726 PRIORITY INFO.: US 1999-09/364,540 19990729

Methods are described for the identification and preparation of ABEN

high-affinity nucleic acid ligands to a VEGF receptor. Included in the invention are specific RNA ligands to a VEGF receptor identified by the SELEX method. Also included are RNA ligands that inhibit the interaction of a VEGF receptor with VEGF.

ABFR

L10 ANSWER 14 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 2000063380 PCTFULL ED 20020515

TITLE (ENGLISH): VASCULAR ENDOTHELIAL CELL GROWTH FACTOR VARIANTS AND

USES THEREOF

VARIANTS DU FACTEUR DE CROISSANCE ENDOTHELIALE ET TITLE (FRENCH):

UTILISATIONS CORRESPONDANTES

CUNNINGHAM, Brian; INVENTOR(S):

ABRAHAM, Devos;

LI, Bing

PATENT ASSIGNEE(S):

GENENTECH, INC.

LANGUAGE OF PUBL.: English Patent

DOCUMENT TYPE:

PATENT INFORMATION:

NUMBER KIND DATE -----WO 2000063380 A1 20001026

Page 25

```
DESIGNATED STATES
                       AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
      W:
                       DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
                       JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
                       MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
                       TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG
                       ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI
                       FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN
                       GW ML MR NE SN TD TG
                       WO 2000-US9483 A 20000410
APPLICATION INFO.:
                       US 1999-60/129,788
PRIORITY INFO.:
                                               19990416
                       US 2000-60/184,235
                                               20000223
ABEN
       The present invention provides VEGF variants having at least a single
       amino acid mutation in
       the native VEGF sequence and selective binding affinity for either the
      KDR receptor or the FLT-1
       receptor. Methods of making the VEGF variants and methods of using the
      VEGF variants are also
      provided.
      La presente invention se rapporte a des variants du VEGF qui presentent
ABFR
      au moins une mutation
      d'acide amine unique dans la sequence du VEGF natif et possedent une
      affinite de liaison selective
       soit pour le recepteur KDR soit pour le recepteur FLT-1. L'invention se
      rapporte egalement a des
       procedes d'elaboration de ces variants VEGF et a des procedes
       d'utilisation de tels variants.
      ANSWER 15 OF 16 PCTFULL
                                  COPYRIGHT 2004 Univentio on STN
L10
ACCESSION NUMBER:
                       1998049300 PCTFULL ED 20020514
                       TRUNCATED VEGF-RELATED PROTEINS
TITLE (ENGLISH):
                       FORMES TRONQUEES DE PROTEINES APPARENTEES AU FACTEUR
TITLE (FRENCH):
                       VEGF
                       BOHLEN, Peter
INVENTOR(S):
PATENT ASSIGNEE(S):
                       COLLATERAL THERAPEUTICS
LANGUAGE OF PUBL.:
                       English
DOCUMENT TYPE:
                       Patent
PATENT INFORMATION:
                       NUMBER
                                          KIND
                                                DATE
                       ______
                       WO 9849300
                                            A2 19981105
DESIGNATED STATES
                       AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE
       W.
                       ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC
                       LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU
                       SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM
                       KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE
                       CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ
                       CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.:
                       WO 1998-US7801
                                            A 19980420
PRIORITY INFO.:
                       US 1997-08/842,984
                                               19970425
ABEN
       The present invention provides novel truncated forms of vascular
       endothelial growth
       factor-related proteins (VRPs or VRPs) which are useful for the
       stimulation of angiogenesis i(in
       vitro) and i(in vivo). The invention also provides nucleic acids
       encoding such novel truncated VRPs
       and methods of producing truncated VRPs. Pharmaceutical compositions
       comprising truncated VRPs and
       methods of gene therapy using the nucleic acids which code for truncated
```

VRPs may be useful for the

treatment of heart disease and for wound healing. ABFR Cette invention se rapporte a de nouvelles formes tronquees de proteines apparentees au facteur de croissance endotheliale vasculaire (VRP) qui servent a stimuler l'engiogenese i(in vitro) et i(in vivo). Cette invention se rapporte egalement a des acides nucleiques codant ces nouvelles proteines VRP tronquees et a des procedes pour produire ces proteines VRP tronquees. Des compositions pharmaceutiques contenant ces proteines VRP tronquees et des procedes de therapie genetique utilisant les acides nucleiques qui codent ces proteines VRP tronquees peuvent servir dans le traitement des maladies cardiaques et pour la cicatrisation des plaies. ANSWER 16 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN L10ACCESSION NUMBER: 1997008313 PCTFULL ED 20020514 VARIANTS OF VASCULAR ENDOTHELIAL CELL GROWTH FACTOR, TITLE (ENGLISH): THEIR USES, AND PROCESSES FOR THEIR PORDUCTION TITLE (FRENCH): VARIANTS DU FACTEUR DE CROISSANCE DES CELLULES DE L'ENDOTHELIUM VASCULAIRE, LEURS UTILISATIONS ET LEURS PROCEDES DE FABRICATION KEYT, Bruce; INVENTOR(S): NGUYEN, Francis, Hung; FERRARA, Napoleone; CUNNINGHAM, Brian, C.; WELLS, James, A.; LI, Bing PATENT ASSIGNEE(S): GENENTECH, INC.; KEYT, Bruce; NGUYEN, Francis, Hung; FERRARA, Napoleone; CUNNINGHAM, Brian, C.; WELLS, James, A.; LI, Bing English LANGUAGE OF PUBL.: DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE WO 9708313 A1 19970306 DESIGNATED STATES AL AM AT AU AZ BB BG BR BY CA CH CN CU CZ DE DK EE ES W: FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US US US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG APPLICATION INFO.: WO 1996-US13621 A 19960823 PRIORITY INFO.: US 1995-60/002,827 19950825 US 1995-8/567,200 19951205 US 1996-8/691,791 19960802 The present invention involves the preparation of vascular endothelial ABEN growth factor (VEGF) variants which provide materials that are selective in respect of binding characteristics to the kinase domain region and the FMS-like tyrosine-kinase region, respectively KDR and FLT-1. The respective KDR and FLT-1 receptors are bound by corresponding domains

within the VEGF compound

domains. The variants hereof define those two binding regions and modify them so as to introduce

changes that interrupt the binding to the respective domain. In this fashion the final biological

characteristics of the VEGF molecule are selectively modified.

La presente invention se rapporte a la preparation de variants du facteur de croissance des

vis a vis des caracteristiques de liaison a la region du domaine kinase  $(\mbox{KDR})$  et a la region

tyrosine kinase de type proteine FMS (FLT-1). Les recepteurs respectifs des regions KDR et FLT-1

sont lies par des domaines correspondants a l'interieur des domaines composes du VEGF. Les variants

de ce facteur definissent ces deux regions de liaison et les modifient de telle sorte que les

modifications introduites interrompent la liaison au domaine respectif. Il est ainsi possible de

modifier selectivement les caracteristiques biologiques finales de la molecule du facteur VEGF.

=>

ABFR

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	115.98	116.19
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY -2.77	SESSION -2.77

STN INTERNATIONAL LOGOFF AT 13:48:32 ON 14 JUN 2004